Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Axitinib

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Axitinib

Dosage Form: Tablet

Route: Oral

Strengths: 1 mg, 5 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 5 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments: Adhere to the following additional comments regarding the study population, exclusion criteria, safety monitoring, stopping rules and informed consent:
   a. Exclusion criteria:
      - Individuals with hepatic, thyroid, or renal dysfunction
      - Current use or anticipated need for drugs with known or suspected interactions with axitinib
      - Subjects with hypertension or cardiovascular risk factors
      - Subjects with a history of gastrointestinal bleeding

   b. Safety monitoring (prior to dosing and after each dosing period) during the bioequivalence study: liver function tests, thyroid function tests, electrocardiogram, urinalysis, and blood pressure. In addition, males with female partners of reproductive potential should use effective contraception during the study and for at least two weeks after the last dose.

c. The following stopping rules are recommended: occurrence of two or more adverse events of >Grade 2 (Common Terminology Criteria for Adverse Events (CTCAE) or WHO Toxicity Criteria), any occurrence of > CTCAE Grade 3 adverse events, or any occurrence of a serious adverse event possibly related to the study drug.

Analyte to measure: Axitinib in plasma

Bioequivalence based on (90% CI): Axitinib

Waiver request of in vivo testing: 1 mg strength based on (i) acceptable bioequivalence study on the 5 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution. Conduct comparative dissolution testing on 12 dosage units for each of both strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the reference listed drug is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*